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DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

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BENZIDINE DYE INITIATIVE -- The NTP benzidine dye initiative is a program that was developed to study the toxicology and carcinogenicity of a class of dyes derived from benzidine, 3,3'-dimethylbenzidine (DMB), or 3,3'-dimethoxybenzidine (DMOB). The objectives and approaches of the initiative were formulated by scientists from EPA, CPSC, OSHA, NIH/NTP, NCTR, and NIOSH in response to the needs of the regulatory agencies. The research per se is a collaborative effort between NIH/NTP, NCTR, and NIOSH, with the Dyes Environmental and Toxicology Organization (DETO) providing chemical consultation and aid in acquiring test materials.

During 1978 the domestic production and import volumes of benzidine dyes totaled 4.1 million pounds (2 million lbs of benzidine-derived, 800,000 lbs of DMB-derived, and 1.3 million lbs of DMOB-derived). An estimated 1,000 workers are exposed to these materials during dye manufacturing and perhaps as many as 15,000 more workers in the various dye application industries. The public is exposed to these materials through contact with finished products (textiles and fabrics), certain packaged dyes for home use, and the use of arts and crafts products (spray paints, enamels, and lacquers) containing benzidine-based dyes.

Benzidine is a carcinogen, causing cancer of the urinary bladder in humans and dogs and hepatocellular carcinoma in rats and mice. Evidence that both DMB and DMOB induce liver tumors in rats prompted the International Agency for Research on Cancer to classify these agents as animal carcinogens. Research reported from several independent studies has demonstrated that in laboratory animals many benzidine and benzidine congener-based dyes are metabolized to their parent amines. This observation suggests that these dyes may be animal carcinogens as well. In fact, three dyes (Direct Blue 6, Direct Black 38, and Direct Brown 95) known to be metabolized to benzidine have produced hepatocellular carcinoma in rats when administered in the diet during a 90-day study (NCI Technical Report No. 108).

Because of the high cost of conducting long-term bioassays, no attempt will be made to test all benzidine and benzidine congener-derived dyes. Instead, a benzidine class toxicology study was designed to develop an integrated body of scientific knowledge concerning the pharmacokinetics and metabolism, genetic toxicology, and in vivo toxicology and carcinogenicity of the benzidine congeners and selected prototypical dyes. Through the judicious selection of chemicals for testing a set of basic principles will be established which can be applied to the entire class of benzidine-based dyes. As designed, this program initiative, summarized in Table 1, will provide much of the scientific information required for making regulatory decisions concerning exposure to the benzidine and benzidine congener-based dyes.

STATUS OF CHEMICALS SELECTED FOR TOXICOLOGICAL TESTING -- In November 1981, the Executive Committee selected 28 chemicals for extensive toxicological characterization. One chemical, Ochratoxin A (CAS No. 303-47-9, chemical manager Dr. W. Eastin) was already on test; another, Naphthalene (CAS No. 91-20-3, chemical manager Dr. S. Brown), was previously tested through the prechronic phase and is now committed to a two-year bioassay. The National Institute for Occupational Safety and Health (NIOSH) and the National Center for Toxicological Research (NCTR) have assumed responsibility for three and five chemicals respectively. Eighteen chemicals have been assigned within the National Institute of Environmental Health Sciences (NIEHS). These chemicals and their chemical manager assignments are listed in Table 2.

Experimental designs and special studies are being prepared by the chemical managers. During the experimental design stage the NTP actively seeks information about these chemicals, especially recently completed, ongoing, or planned studies by other organizations. Persons having additional information are requested to contact the designated chemical manager (for address see Table 2). Questions on the testing status of these chemicals should be addressed to Ms. Joan Chase, National Toxicology Program, 7910 Woodmont Ave., Landow 3A06, Bethesda, MD 20205, 301-496-1152, FTS 8-496-1152.

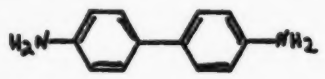
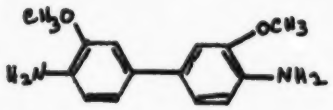
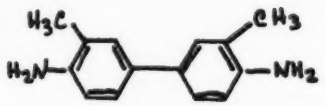
RAPID IN VITRO TEST CAPABILITIES -- Short-term tests and combinations of tests have been proposed to predict the potential carcinogenicity of chemicals. However, current data are not sufficient, particularly across chemical classes, to correlate short-term test results with known carcinogenicity so that the limits of predictability can be accurately judged. A primary emphasis of the Cellular and Genetic Toxicology Branch is to develop, evaluate, and validate test systems which will contribute to a data base that should permit clear decisions about the relative value of a proposed test. To serve the broader objectives of the NTP, it is important to provide short-term test information which can be used by the experimental design groups and for establishing the priority of chemicals to be entered into long-term carcinogenicity bioassays. The five broad classes of in vitro short-term tests are:

1. gene mutations in bacteria -- Salmonella typhimurium/microsome
2. gene mutations in mammalian cells -- mouse lymphoma (L5178Y, thymidine kinase)
3. chromosome damage in mammalian cells -- cytogenetic damage and sister chromatid exchange (in vitro, CHO)
4. a mammalian cell transformation assay -- (BALB/c-3T3)
5. a direct measure of DNA damage/repair (which does not necessarily result in mutation or transformation) -- unscheduled DNA synthesis (rat hepatocytes)

This group of tests was chosen because the basic categories of genotoxic effects can be detected, the tests are readily available, and the accepted protocols have been subjected to some form of evaluation or validation. At present there is inadequate evidence to select or justify any specific assay system as a prescreen for carcinogens or mutagens. The use of the above group should not be interpreted as a position on the part of the NTP of endorsing any specific battery of biologically based tests. Rather, it is intended that the results provide a reasonable profile of the genetic toxicity of a chemical.

TABLE 1

SUMMARY OF THE NTP BENZIDINE CONGENER INITIATIVE

Chemical	Tests[1]	Parent Structure
Benzidine derived		
Benzidine	G, P, B[2]	
C.I. Direct Blue 6	G, P, B[2]	
o-Dianisidine derived (3,3'-dimethoxybenzidine)		
o-dianisidine	G, P, B[3]	
C.I. Direct Black 114	G, M	
C.I. Direct Blue 8	G, M	
C.I. Direct Blue 15	G, P, B[3]	
C.I. Direct Blue 218	G, P, B[4]	
C.I. Direct Violet 32	G, M	
o-Tolidine derived (3,3'-dimethylbenzidine)		
o-tolidine	G, P, B[3]	
C.I. Acid Red 114	G, P, B[3]	
C.I. Direct Blue 14	G	
C.I. Direct Blue 25	G	
C.I. Direct Blue 53	G, M	
C.I. Direct Orange 6	G, M	
C.I. Direct Red 2	G, M	
C.I. Direct Red 39	G, M	

[1] Key: G = Genetic toxicology testing
P = Pharmacokinetic studies
M = Metabolism studies for detection of carcinogens in urine
B = Toxicologic and carcinogenesis bioassay

[2] Benzidine and Direct Blue 6 are being comparatively studied in a 90-day feeding study in rats only.

[3] o-Tolidine, Acid Red 114, o-Dianisidine and Direct Blue 15 are being comparatively evaluated in a standard bioassay in rats only.

[4] Direct Blue 218 is scheduled for testing in rats and mice in a 90-day study. Data from this study and genetic toxicology and pharmacokinetic studies will be used to determine the need for a two-year bioassay.

TABLE 2

CHEMICALS SELECTED FOR TOXICOLOGICAL TESTING

Chemical	CAS Registry No.	NTP Chemical Manager
2-Bromo-4,6-Dinitroaniline	1817-73-8	Dr. K. Chu, NIEHS[4]
beta-Bromo-beta-Nitrostyrene	7166-19-0	Dr. H. Weber, NIEHS[3]
C.I. Direct Yellow 11	1325-37-7	Dr. W. Eastin, NIEHS[3]
C.I. Vat Blue 1	482-89-3	Dr. J. Mennear, NIEHS[3]
Cadmium Nitrate	10325-94-7	Dr. J. Dunnick, NIEHS[3]
Carisoprodol	78-44-4	Dr. J. Douglas, NIEHS[4]
1,3-Dichloro-5,5-Dimethyl-hydantoin	118-52-5	Dr. D. Roberts, NCTR[1]
1,8-Dihydroxy-4,5-Dinitro-anthraquinone	81-55-0	Dr. R. Irwin, NIEHS[3]
2,4-Dinitroaniline	97-02-9	Dr. J. Hinson, NCTR[1]
Estragole	140-67-0	Mr. G. Cronin, NCTR[1]
Ethyl Benzene	100-41-6	Dr. H. Plotnick, NIOSH[2]
n-Hexane	110-54-3	Dr. J. Dunnick, NIEHS[3]
1,6-Hexanediamine	124-09-4	Dr. G. Wolff, NCTR[1]
Isobutyraldehyde	78-84-2	Dr. J. McCoy, NIEHS[4]
N-Isopropyl-N'-Phenyl-p-Phenylenediamine	101-72-4	Dr. F. Kadlubar, NCTR[1]
2-Mercaptobenzimidazole	583-39-1	Dr. J. Quest, NIEHS[4]
Methyl Bromide	74-83-9	Dr. K. Chu, NIEHS[4]
Molybdenum Trioxide	1313-27-5	Dr. J. Quest, NIEHS[4]
d-Phenylalanine	673-06-3	Dr. K. Abdo, NIEHS[3]
Polyvinyl Chloride Latex	9002-86-2	NIEHS[3]
Sucrose	57-50-1	Dr. Whitmire, NIEHS[4]
Talc	14807-96-6	Dr. S. Brown, NIEHS[4]
alpha-Tocopherol (Vitamin E)		Dr. K. Abdo, NIEHS[3]
1-Trans-delta(9)-Tetrahydro-cannabinol	1972-08-3	Dr. D. Goldman, NIEHS[4]
Vanadium Pentoxide	1314-62-1	Dr. R. Niemeier, NIOSH[2]
Zinc Oxide	1314-13-2	Dr. W. Moorman, NIOSH[2]

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[1]National Center for Toxicological Research, Jefferson, AK 72079
[2]National Institute for Occupational Safety and Health, Taft Laboratories C22, 4676 Columbia Parkway, Cincinnati, OH 45226
[3]National Institute of Environmental Health Sciences, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709
[4]National Institute of Environmental Health Sciences, National Toxicology Program, Landow Building, Room 3C-25, 7910 Woodmont Avenue, Bethesda, MD 20205

MUTAGENESIS TESTING RESULTS -- Results from the Salmonella typhimurium assay on an additional 99 coded chemicals appear in Table 3.

BOARD OF SCIENTIFIC COUNSELORS -- The NTP Board met on October 22 and 23, 1981 at the National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio. Coordinator for this meeting was Dr. Barry L. Johnson, Director, Division of Biomedical and Behavioral Sciences, NIOSH.

The first day focused on peer review of NTP programs at NIOSH and NIEHS in inhalation toxicology (Dr. T. Lewis, NIOSH and Dr. E. Van Stee, NIEHS) and neurobehavioral toxicology (Dr. W.K. Anger, NIOSH and Dr. H. Tilson, NIEHS). Ad hoc consultants joining the Board were: Dr. J. Douglas MacEwen, University of Califorina, Irvine, and Dr. Michael McKenna, Dow Chemical Company (inhalation toxicology); Dr. Stata Norton, University of Kansas, and Dr. John Repko, University of Arizona (neurobehavioral toxicology).

Other highlights of the meeting included:

- Concept Review -- The Board approved the concepts for one new initiative and two continuing activities: Salmonella Mutagenicity Testing; Recompetition of Mammalian Cell (L5178Y Mouse Lymphoma TK +/-) Mutagenesis Assay Contracts; and Assay of Chemicals for Induction of Heritable Translocations.

- Peer Review and Priority Ranking of Chemicals Nominated for NTP Testing --The Board reviewed twenty-six chemicals which had been nominated for testing and previously evaluated by the NTP Chemical Evaluation Committee. The Board's recommendations and priority rankings have been incorporated into the final literature summaries sent to the NTP Executive Committee.

- Categorizing Bioassay Results as to Strength of Evidence for Carcinogencity in Animals -- Dr. A. Whittemore described a draft "decision tree" approach employing six categories. The Board recommended that NTP use the categories on a trial basis for the peer review of draft technical reports of carcinogenesis bioassays.

The next meeting of the Board of Scientific Counselors will be held on March 10-12, 1982, in the South Campus Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. Specific areas to be reviewed and evaluated are (a) the design and conduct of the two-year rodent bioassays and (b) the utility of short term in vivo tumor systems in carcinogenicity testing. The Board members will be augmented by an ad hoc working group of international scientists expert in chemical mutagenesis and carcinogenesis.

Those interested in attending or learning more about the meeting should contact Dr. Larry Hart, National Toxicology Program, P.O. Box 12233, Research Triangle Park, North Carolina 27709, telephone 919-541-3989; FTS 629-3989. An announcement with further details and agenda topics will be published in the Federal Register. Requests for summary minutes of the Board meetings should also be directed to Dr. Hart.

CARCINOGENESIS BIOASSAY RESULTS -- On December 16, the NTP Board of Scientific Counselors Technical Reports Peer Review Subcommittee evaluated and approved the results of five carcinogenesis bioassays. Acceptance of the Propyl Gallate bioassay was deferred pending a reevaluation of the results. Abbreviated details from these reports appear in Table 4.

The next meeting of the Panel is scheduled for June 1982 (date and location to be announced in the April Bulletin). Technical Reports to be evaluated include: Ascorbic Acid, Benzyl Acetate, Diallyl Phthalate, Melamine, 4,4'-Methylenedianiline Dihydrochloride, and Trichloroethylene.

TABLE 3. NTP Mutagenesis (Salmonella typhimurium) Test Results (a)

	1 CHEMICAL NAME (b)	2 CAS #	3 LAB (c)	4 RESULTS (d)
1	1-ACETYL-2-PICOLINOYL HYDRAZINE	17433-31-7	[SRI]	[-]
2	ACETYL-O-TOLUIDINE	120-66-1	[EGG]	[+W]
3	ADIPAMIDE	628-94-4	[CWR]	[-]
4	ALLYL GLYCIDYL ETHER	106-92-3	[EGG]	[+]
5	ALLYL ISOVALERATE	2835-39-4	[CWR]	[-]
6	ARIBEN	133-90-4	[CWR]	[+]
7	1-AMINO-2,4-DIBROMO ANTHRAQUINONE	81-49-2	[SRI]	[+]
8	3-AMINO-4-ETHOXY-ACETANILIDE	17026-81-2	[CWR]	[+]
9	3-AMINO-9-ETHYLCARBAZOLE HCL	6109-97-3	[CWR]	[+]
10	11-AMINOUNDECANOIC ACID	27323-47-3	[SRI]	[-]
11	AMPICILLIN TRIHYDRATE	7177-48-2	[EGG]	[-]
12	BENZYL ACETATE	140-11-4	[CWR]	[-]
13	2-BUTANONE PEROXIDE	1338-23-4	[SRI]	[-]
14	TERT-BUTYL ALCOHOL	75-65-0	[CWR]	[-]
15	BUTYLATED HYDROXYTOLUENE (BHT)	128-37-0	[EGG]	[-]
16	TERT-BUTYL HYDROPEROXIDE	75-91-2	[CWR]	[+]
17	CADMIUM CHLORIDE	10108-64-2	[EGG]	[-]
18	2-CHLORO-1,3-BUTADIENE	126-99-8	[SRI]	[-]
19	2-CHLOROETHYL TRIMETHYL AMMONIUM CL (CCC)	999-81-5	[SRI]	[-]
20	CROTON OIL	8001-28-3	[CWR]	[-]
21	CYTOXAL ALCOHOL	4466-84-5	[CWR]	[+]
22	DECABROMODIPHENYL OXIDE	1163-19-5	[SRI]	[-]
23	DIALLYL PHTHALATE	131-17-9	[CWR]	[-]
24	4,4'-DIAMINO-2,2'-STILBENEDISULFONIC ACID	81-11-8	[EGG]	[-]
25	DIBUTYL PHTHALATE	84-74-2	[EGG]	[-]
26	TRANS-1,2-DICHLOROETHYLENE	156-60-5	[SRI]	[-]
27	1,3-DICHLOROPROPENE	542-75-6	[SRI]	[+]
28	DICOFOL	115-32-2	[CWR]	[-]
29	DIESEL FUEL-MARINE		[EGG]	[-]
30	DI(2-ETHYLHEXYL)ADIPATE	103-23-1	[EGG,SRI]	[-,-]
31	DIISODECYL PHTHALATE	26761-40-0	[FRI]	[-]
32	DIMETHOATE (CYGON)	60-51-5	[SRI,CWR]	[+,+]
33	DIMETHYL METHYLPHOSPHONATE	756-79-6	[EGG]	[-]
34	N,N-DIMETHYL-P-NITROSOANILINE	138-89-6	[EGG]	[+]
35	DIMETHYL PHTHALATE	131-11-3	[EGG]	[-]
36	DIMETHYL VINYL CHLORIDE	513-37-1	[CWR]	[-]
37	4,4'-DIPHENYLMETHANE DIISOCYANATE	101-68-8	[CWR]	[-]
38	8,8-DITHIODIUREA	142-46-1	[CWR]	[-]
39	DULCIN	150-69-6	[CWR]	[-]
40	1,2-EPOXYBUTANE	106-88-7	[SRI]	[+]
41	ETHYL ACRYLATE	140-88-5	[SRI,CWR]	[-,-]
42	FLUORESCEIN, 2NA	518-47-8	[CWR]	[-]
43	GERANYL ACETATE	105-87-3	[CWR]	[-]
44	N-HEXANE	110-54-3	[EGG]	[-]
45	ISOPHORONE	78-59-1	[CWR]	[-]
46	LEAD DIMETHYL DITHIOCARBAMATE (LEDATE)	19010-66-3	[SRI]	[+]
47	D-LIMONENE	5989-27-5	[SRI]	[-]
48	LINOLEIC ACID	60-33-3	[EGG]	[-]
49	MELAMINE	108-78-1	[CWR]	[-]
50	MERCURIC CHLORIDE	7487-94-7	[EGG]	[-]
51	N-METHYL-P-AMINOPHENOL SULFATE	55-55-0	[CWR]	[+W]
52	ALPHA METHYLBENZYL ALCOHOL	98-85-1	[EGG]	[-]
53	2-METHYL-1-NITROANTHRAQUINONE	129-15-7	[SRI]	[+]
54	3-METHYL-3-PHENYLGLYCIDIC ACID, ETHYL ESTER	77-83-8	[CWR]	[-]
55	NAPHTHALENE	91-20-3	[EGG]	[-]
56	NAVY FUEL JP-5		[SRI]	[-]
57	NITHIAZIDE	139-94-6	[EGG]	[+]
58	3'-NITROACENAPHTHENE	602-87-9	[EGG]	[+]
59	6-NITROBENZIMIDAZOLE	94-52-0	[EGG]	[+]
60	NITROFURAZONE	59-87-0	[SRI]	[+]
61	OLEIC ACID	112-80-1	[EGG]	[-]
62	OLEIC ACID METHYL ESTER (CIS)	112-62-9	[EGG]	[-]
63	OXYTETRACYCLINE HCL	2058-46-0	[EGG]	[-]
64	PALLADIUM (II) CHLORIDE	7647-10-1	[SRI]	[-]
65	PENICILLIN VK	132-98-9	[CWR]	[-]
66	PENTACHLOROETHANE	76-01-7	[SRI]	[-]
67	PHENIRAMINE MALEATE	132-20-7	[SRI]	[-]
68	PHENOL	108-95-2	[EGG,EGG]	[-,-]
69	N-PHENYLHYDROXYLAMINE	100-65-2	[EGG]	[+]
70	PHENYL MERCURIC ACETATE	62-38-4	[SRI,CWR]	[-,-]
71	O-PHENYLPHENOL	90-43-7	[EGG]	[+W]
72	N-PHENYL-P-PHENYLENEDIAMINE	101-54-2	[SRI]	[-]
73	1-PHENYL-2-THIOUREA	103-85-5	[SRI]	[-]
74	1(2H)-PHTHALAZINONE	119-39-1	[EGG]	[-]
75	POLYSORBATE 80 (TWEEN 80)	9005-65-6	[EGG]	[-]
76	PREDNISONE	53-03-2	[SRI]	[+W]
77	PROBENECID	57-66-9	[CWR]	[-]
78	PROPYL GALLATE	121-79-9	[SRI]	[-]
79	PYRIMETHAMINE	58-14-0	[CWR]	[-]
80	ROTENONE	83-79-4	[SRI]	[-]
81	SODIUM ALUMINOSILICATE	1344-00-9	[EGG]	[-]
82	SODIUM DODECYL SULFATE	151-21-3	[SRI]	[-]
83	STREPTOMYCIN SULFATE (2:3)	3810-74-0	[SRI,CWR,EGG]	[+W,-,+W]
84	SUCCINIC ACID 2,2-DIMETHYLHYDRAZIDE	1596-84-5	[EGG]	[-]
85	3-SULFOLENE	77-79-2	[CWR]	[-]
86	TCDD (2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN)	1746-01-6	[SRI]	[-]
87	1,2,4,5-TETRACHLOROBENZENE	95-94-3	[EGG]	[-]
88	1,1,2,2-TETRACHLOROETHANE	79-34-5	[CWR]	[-]
89	TETRAKIS HYDROXYMETHYL PHOSPHONIUM CL	124-64-1	[CWR]	[-]
90	TETRAMETHYLLEAD	75-74-1	[SRI]	[-]
91	P-TOLYLUREA	622-51-5	[SRI]	[-]
92	1,2,3-TRICHLOROPROPANE	96-18-4	[SRI]	[+]
93	TRIHYDROXYBUTYROPHENONE	1421-63-2	[CWR]	[+]
94	TRIS(2-ETHYLHEXYL)PHOSPHATE	78-42-2	[CWR]	[-]
95	UREA	57-13-6	[SRI]	[-]
96	4-VINYLCYCLOHEXENE	100-40-3	[CWR]	[-]
97	1-VINYL-3-CYCLOHEXENE DIOXIDE	106-87-6	[SRI]	[+]
98	XYLENESULFONIC ACID, NA SALT	1300-72-7	[CWR]	[-]
99	ZIRAM	137-30-4	[SRI]	[+]

(a) = Test conditions: male Sprague-Dawley rat and Syrian hamster liver activation (Arochlor 1254) and preincubation suspension; (b) = Chemicals were coded randomly and tested as unknowns; (c) = CWR = Case Western Reserve University, Cleveland, OH (Dr. William Speck), EGG = EG&G Mason Research Institute, Rockville, MD (Dr. Steven Haworth), SRI = SRI International, Menlo Park, CA (Dr. Kristien Mortelmans); (d) = Certain chemicals, randomly selected, which may have appeared before, were tested at more than one laboratory.

NTP/NCI CARCINOGENESIS BIOASSAY TECHNICAL REPORTS

Copies of the following NTP/NCI Carcinogenesis Bioassay Technical Reports (TR) may be requested (while supplies last) from Ms. Joan Chase, Technical Information, National Toxicology Program, Room A306 Landow Building, 7910 Woodmont Avenue, Bethesda, MD 20205. Priority for complete sets will be given to libraries. For individual requests an address label for every five reports is necessary to expedite handling. Allow 6 to 8 weeks for shipping.

CHEMICAL	CAS NO.	TR NO.
Acetohexamide	968-81-0	50
Acronycine	7008-42-6	49
Actinomycin D	50-76-0	a
Aldicarb	116-06-3	136
Aldrin	309-00-2	21
Allyl Chloride	107-05-1	73
2-Aminoanthraquinone	117-79-3	144
3-Amino-4-Ethoxyacetanilide	17026-81-2	112
3-Amino-9-Ethylcarbazole Hydrochloride	132-32-1	93
1-Amino-2-Methylanthraquinone	82-28-0	111
4-Amino-2-Nitrophenol	119-34-6	94
2-Amino-5-Nitrothiazole	121-66-4	53
Anilazine	101-05-3	104
Aniline Hydrochloride	142-04-1	130
o-Anisidine Hydrochloride	134-29-2	89
p-Anisidine Hydrochloride	20265-97-8	116
o-Anthranilic Acid	118-92-3	36
Arochlor-1254	11097-69-1	38
Aspirin, Phenacetin, And Caffeine	8003-03-0	67
5-Azacytidine	320-67-2	42
Azathioprine	446-86-6	a
Azinphosmethyl	86-50-0	69
Azobenzene	103-33-3	154
Benzoin	119-53-9	204
1H-Benzotriazole	95-14-7	88
1,3-Bis(Chloroethyl)-1-Nitrosourea	154-93-8	a
Bis(2-Chloro-1-Methylethyl) Ether	108-60-1	191
Butylated Hydroxytoluene (BHT)	128-37-0	150
Calcium Cyanamide	156-62-7	163
Caprolactam	105-60-2	214
Captan	133-06-2	15
Carbromal	77-65-6	173
Chloramben	133-90-4	25
Chlorambucil	305-03-3	a
Chlordane	12789-03-6	8
Chlordecone	143-50-0	b
4'-(Chloroacetyl)-Acetanilide	140-49-8	177
p-Chloroaniline	106-47-8	189
Chlorobenzilate	510-15-6	75
(2-Chloroethyl) Trimethylammonium Chloride	999-81-5	158
Chloroform	67-66-3	c
2-(Chloromethyl)Pyridine Hydrochloride	6959-47-3	178
3-(Chloromethyl)Pyridine Hydrochloride	6959-48-4	95
4-Chloro-m-Phenylenediamine	5131-60-2	85
4-Chloro-o-Phenylenediamine	95-83-0	63
2-Chloro-p-Phenylenediamine Sulfate	61702-44-1	113
Chloropicrin	76-06-2	65
Chlorothalonil	1897-45-6	41
4-Chloro-o-Toluidine Hydrochloride	3165-93-3	165
5-Chloro-o-Toluidine	95-79-4	187
3-Chloro-p-Toluidine	95-74-9	145
Chlorpropamide	94-20-2	45
Cinnamyl Anthranilate	87-29-6	196
C.I. Vat Yellow 4	128-66-5	134
Clonitralid	1420-04-8	91
Coumaphos	56-72-4	96
m-Cresidine	102-50-1	105
p-Cresidine	120-71-8	142
Cupferron	135-20-6	100
Cyclophosphamide	50-18-0	a
Cytarabine	147-94-4	a
Cytembena	21739-91-3	207
Cytoxyl Alcohol	4465-94-5	a
Dacarbazine	4342-03-4	a
Dapsone	80-08-0	20
Daunomycin	20830-81-3	a
o,p'-DDD	53-19-0	a
p,p'-DDE	72-55-9	131
DDT	50-29-3	131
2,4-Diaminoanisole Sulfate	39156-41-7	84
2,4-Diaminotoluene	95-80-7	162
Diaminozide	1596-84-5	83
Diarylanilide Yellow	6358-85-6	30
Diazinon	333-41-5	137
Dibenzo-p-Dioxin	262-12-4	122
Dibromochloropropane	96-12-8	28
Dibromodulcitol	10318-26-0	a
1,2-Dibromoethane	106-93-4	86
Dibromomannitol	488-41-5	a
Dibutyltin Diacetate	1067-33-0	183
2,7-Dichlorodibenzo-p-Dioxin (DCDD)	33857-26-0	123
1,1-Dichloroethane	75-34-3	66
1,2-Dichloroethane	107-06-2	55
Dichloromethotrexate	528-74-5	a
Dichlorvos	62-73-7	10
Dicofol	115-32-2	90
N,N'-Dicyclohexylthiourea	1212-29-9	56
Dieldrin	60-57-1	21
Dieldrin	60-57-1	22
Di(2-Ethylhexyl)Adipate	103-23-1	212
N,N'-Diethylthiourea	105-55-5	149
Dimethoate	60-51-5	4
2,4-Dimethoxyaniline Hydrochloride	54150-69-5	171
3,3'-Dimethoxybenzidine-4, 4'-Diisocyanate	91-93-0	128
Dimethyl Terephthalate	120-61-6	121
2,4-Dinitrotoluene	121-14-2	54
1,4-Dioxane	123-91-1	80
Dioxathion	78-34-2	125
Direct Black 38	1937-37-7	108
Direct Blue 6	2602-46-2	108
Direct Brown 95	16071-86-6	108
2,5-Dithiobiurea	142-46-1	132
EDTA (Trisodium Ethylenediamine tetraacetate T	150-38-9	11
Emetine	483-18-1	43
Endosulfan	115-29-7	62
Endrin	72-20-8	12
Estradiol Mustard	22966-79-6	59
Ethionamide	536-33-4	46
p,p-Ethyl DDD (Perthane)	72-56-0	156
Ethyl Tellurac	20941-65-5	152
FD&C Yellow 6	2783-94-0	208
Fenthion	55-38-9	103
Fluometuron	2164-17-2	195
Formulated Fenaminosulf	140-56-7	101
Guanazole	1455-77-2	a
Heptachlor	76-44-8	9
1,2,3,6,7,8-Hexachlorodibenzo-p-dioxin	57653-85-7	198
1,2,3,6,7,8-Hexachlorodibenzo-p-dioxin	57653-85-7	202

CHEMICAL	CAS NO.	TR NO.
Hexachloroethane	67-72-1	68
Hexachlorophene	70-30-4	40
Hydrazobenzene	122-66-7	92
Hydroxyurea	127-07-1	a
ICRF-159	21416-87-5	78
Iodoform	75-47-8	110
IPD (3,3'-Iminobis-1-Propanol Dimethylsulfone	3458-22-8	18
Isophosphamide	3778-73-2	32
Lasiocarpine	303-34-4	39
Lead Dimethyldithiocarbamate	19010-66-3	151
Lindane	58-89-9	14
Lithocholic Acid	434-13-9	175
Lomustine	13010-47-4	a
Malaoxon	1634-78-2	135
Malathion	121-75-5	24
Malathion	121-75-5	192
Melphalan	148-82-3	a
dl-Menthol	15356-70-4	98
6-Mercaptopurine	50-44-2	a
Merphalan	531-76-0	a
Methotrexate	59-05-2	a
Methoxychlor	72-43-5	35
Methyl CCNU	13909-09-6	a
4,4'-Methylenebis(N,N-Dimethyl)Benzenamine	101-61-1	186
6-Methylmercaptopurine Ribonucleoside	342-69-8	a
2-Methyl-1-Nitroanthraquinone	129-15-7	29
2-Methyl-1-Nitroanthraquinone	129-15-7	d
Methyl Parathion	298-00-0	157
Mexacarbate	315-18-4	147
Michler's Ketone	90-94-8	181
Mitomycin C	50-07-7	a
1,5-Naphthalenediamine	2243-62-1	143
N-(1-Naphthyl)Ethylenediamine.2HCl	1465-25-4	168
Nithiazide	139-94-6	146
Nitrilotriacetic Acid (NTA)	139-13-9	6
5-Nitroacenaphthene	602-87-9	118
3'-Nitro-p-Acetophenetide	1777-84-0	133
5-Nitro-o-Anisidine	99-59-2	127
4-Nitroanthranilic Acid	619-17-0	109
6-Nitrobenzimidazole	94-52-0	117
Nitrofen	1836-75-5	184
Nitrofen	1836-75-5	26
1-Nitronaphthalene	86-57-7	64
4-Nitro-o-Phenylenediamine	99-56-9	180
2-Nitro-p-Phenylenediamine	5307-14-2	169
3-Nitropropionic Acid	504-88-1	52
N-Nitrosodiphenylamine	86-30-6	164
P-Nitrosodiphenylamine	156-10-5	190
Beta-Nitrostyrene and Styrene	102-96-5	170
5-Nitro-o-Toluidine	99-55-8	107
NTA (Nitrilotriacetic Acid) and Nitrilotriacetic Acid Trisodium Salt	139-13-9 18662-53-8	6
4,4'-Oxydianiline	101-80-4	205
Parathion	56-38-2	70
Pentachloronitrobenzene	82-68-8	61
Phenazopyridine Hydrochloride	136-40-3	99
Phenesterin	3546-10-9	60
Phenformin	114-86-3	7
Phenol	108-95-2	203

CHEMICAL	CAS NO.	TR NO.
Phenoxybenzamine Hydrochloride	63-92-3	72
p-Phenylenediamine Dihydrochloride	624-18-0	174
1-Phenyl-3-Methyl-5-Pyrazolone	89-25-8	141
N-Phenyl-p-Phenylenediamine	101-54-2	82
1-Phenyl-2-Thiourea	103-85-5	148
Phosphamidon	13171-21-6	16
Photodieldrin	13366-73-9	17
Phthalamide	88-96-0	161
Phthalic Anhydride	85-44-9	159
Picloram	1918-02-1	23
Piperonyl Butoxide	51-03-6	120
Piperonyl Sulfoxide	120-62-7	124
Pivalolactone	1955-45-9	140
Prednisone	53-03-2	a
Procarbazine	366-70-1	a
Procarbazine	366-70-1	19
Proflavine	952-23-8	5
Pyrazinamide	98-96-4	48
Pyrimethamine	58-14-0	77
p-Quinone Dioxime	105-11-3	179
Reserpine	50-55-5	193
Sodium Diethyldithiocarbamate	148-18-5	172
Streptozoticin	18883-66-4	a
Styrene	100-42-5	185
Sulfallate	95-06-7	115
Sulfisoxazole	127-69-5	138
3-Sulfolene	77-79-2	102
TDE	72-54-8	131
1,1,2,2-Tetrachloroethane	79-34-5	27
Tetrachloroethylene	127-18-4	13
2,3,5,6-Tetrachloro-4-Nitroanisole	2438-88-2	114
Tetrachlorvinphos	961-11-5	33
Tetraethylthiuram Disulfide	97-77-8	166
B-TGDR	789-61-7	57
4,4'-Thiodianiline	139-65-1	47
Thio-TEPA	52-24-4	58
Titanium Dioxide	13463-67-7	97
Tolazamide	1156-19-0	51
Tolbutamide	64-77-7	31
2,6-Toluenediamine Dihydrochloride	15481-70-6	200
2,5-Toluenediamine Sulfate	6369-59-1	126
o-Toluidine Hydrochloride	636-21-5	153
Toxaphene	8001-35-2	37
1,1,1-Trichloroethane	71-55-6	3
1,1,2-Trichloroethane	79-00-5	74
Trichloroethylene	79-01-6	2
Trichlorofluoromethane	75-69-4	106
2,4,6-Trichlorophenol	88-06-2	155
Trifluralin	1582-09-8	34
2,4,5-Trimethylaniline	137-17-7	160
Trimethylphosphate	512-56-1	81
Trimethylthiourea	2489-77-2	129
Triphenyltin Hydroxide	76-87-9	139
Tris (2,3-Dibromopropyl) Phosphate	126-72-7	76
l-Tryptophan	73-22-3	71
Uracil Mustard	66-75-1	a
Vinblastine	865-21-4	a
Vincristine	57-22-7	a

a = Cancer, 1977, Vol. 40, pp 1935-1949; b = NCI Brief Communication; c = No TR number assigned; d = A.S. Krishna Murthy et al., Int. J. Cancer, 1977, Vol. 19, pp 117-121.

TABLE 4

NTP TOXICOLOGY AND CARCINOGENESIS BIOASSAY RESULTS

CHEMICAL/CAS NTP NUMBER	NTP/TR REPORT NO. -- PEER REVIEW DATE (P = PUBLISHED)	USE	ROUTE/DOSE	CONTRACT LABORATORY	NTP CHEMICAL MANAGER	RESULTS UNDER THE CONDITIONS OF THESE TESTS (* = STATISTICALLY SIGNIFICANT) (P < 0.05)
BIS(2-CHLORO-1-METHYL ETHYL)ETHER (BCMEE) 108-60-1 10523-N	NTP-81-055 TR-239 12/16/81	PAINT & VARNISH REMOVERS: INTERMEDIATE IN DYES,RESINS AND PHARMACEUTICALS MANUFACTURE; AND NEMATOCIDE IN JAPAN	GAVAGE (CORN OIL) 5 TIMES/ WEEK: MICE-- 100, OR 200 MG/KG	EG&G MASON RESEARCH INSTITUTE	DR. M. POWERS	CARCINOGENIC FOR B6C3F1 MICE CAUSING ALVEOLAR/BRONCHIOLAR ADENOMAS IN MALES (5/50, 13/50*, 11/50) AND IN FEMALES (1/50, 4/50, 8/50*) AND INDUCING IN MALES DOSE-RELATED HEPATOCELLULAR CARCINOMAS (5/50, 13/50, 17/50*). RARE FORESTOMACH TUMORS WERE PROBABLY ASSOCIATED WITH THE TEST CHEMICAL (LOW DOSE: 1 MALE; HIGH DOSE: 2 MALES AND 3 FEMALES).
D-MANNITOL 69-65-8 10368-L	NTP-81-052 TR-236 12/16/81	CHEWABLE TABLETS, SUGAR REPLACEMENT, CANDIES AND GUMS, OSMOTIC DIURETIC, AND FLUID REPLACEMENT	FEED: 25,000 OR 50,000 PPM	SOUTHERN RESEARCH INSTITUTE	DR. K. M. ABDO	NOT CARCINOGENIC FOR F344 RATS OF B6C3F1 MICE OF EITHER SEX.
PROPYL GALLATE 121-79-9 10564-Y	NTP-81-042 TR-240 12/16/81	ANTIOXIDANT IN FOODS CONTAINING FATS/OILS, IN FOOD-PACKAGING AND IN COSMETICS	FEED: 6,000 OR 12,000 PPM	SOUTHERN RESEARCH INSTITUTE	DR. K. M. ABDO	NOT CONSIDERED CARCINOGENIC FOR F344 RATS, ALTHOUGH THERE WAS EVIDENCE OF AN INCREASED NUMBER OF MALE RATS WITH PREPUTIAL GLAND TUMORS (1/50, 8/50*, 0/50), ISLET-CELL ADENOMAS OF THE PANCREAS (0/50, 6/50*, 2/50), AND PHEOCHROMOCYTOMAS OF THE ADRENAL GLANDS (4/50, 13/48*, 6/50); RARE TUMORS OF THE BRAIN OCCURRED IN FEMALE RATS (0/50, 3/50, 0/49). NOT CARCINOGENIC FOR B6C3F1 MICE OF EITHER SEX, ALTHOUGH THE INCREASED NUMBER OF MALE MICE WITH MALIGNANT LYMPHOMA (1/50, 3/49, 8/50*) MAY HAVE BEEN ASSOCIATED WITH THE ADMINISTRATION OF PROPYL GALLATE.
1,1,1,2-TETRACHLOROETHANE 630-20-6 10651-J	NTP-81-053 TR-237 12/16/81	CHEMICAL INTERMEDIATE FOR PRODUCING TRI- AND TETRA-CHLOROETHYLENE	GAVAGE (CORN OIL) 5 TIMES/ WEEK: RATS -- 125 OR 250 MG/KG; MICE -- 250 OR 500 MG/KG	GULF SOUTH RESEARCH INSTITUTE	DR. L. BIRNBAUM	NOT DEMONSTRATED CARCINOGENIC FOR F344 RATS (INCREASED INCIDENCE OF COMBINED NEOPLASTIC NODULES AND HEPATOCELLULAR CARCINOMAS IN MALES 0/49, 1/49, 3/48 AND FIBROADENOMAS OF MAMMARY GLAND IN FEMALES 6/49, 15/49*, 7/46 MAY HAVE BEEN ASSOCIATED WITH TEST CHEMICAL). CARCINOGENIC IN B6C3F1 MICE (HEPATOCELLULAR CARCINOMAS - FEMALES: 1/49, 5/46, 6/48*; HEPATOCELLULAR ADENOMAS - MALE: 6/48, 14/48*, 21/50*; FEMALES 4/49, 6/46, 24/48*).
ZEARALENONE 17924-92-4 10770-C	NTP-81-037 TR-235 12/16/81	NON-STEROID ESTROGENIC MYCOTOXIN (ANABOLIC STEROID)	FEED: RATS -- 25 OR 50 PPM; MICE -- 50 OR 100 PPM	SOUTHERN RESEARCH INSTITUTE	DR. D. GOLDMAN	NOT CARCINOGENIC FOR F344 RATS OF EITHER SEX; SHOULD BE CONSIDERED CARCINOGENIC FOR B6C3F1 MICE (MALE: PITUITARY ADENOMA 0/40,4/45, 6/44*; FEMALE: PITUITARY ADENOMA 3/46, 2/43, 13/42*; HEPATOCELLULAR ADENOMA 0/50, 2/49, 7/49*).
ZIRAM (ZINC DIMETHYLDITHIO CARBAMATE) 137-30-4 10590-G	NTP-81-057 TR-238 12/16/81	FUNGICIDE AND ACCELERATOR IN RUBBER VULCANIZATION	FEED: RATS -- 300 OR 600 PPM; MICE -- 600 OR 1200 PPM	SOUTHERN RESEARCH INSTITUTE	DR. D. GOLDMAN	CARCINOGENIC FOR MALE F344 RATS CAUSING C-CELL CARCINOMAS OF THE THYROID 0/50, 2/49, 7/49*; NOT CARCINOGENIC FOR FEMALE F344 RATS OR FOR MALE B6C3F1 MICE; INTERPRETATION OF THE INCREASED NUMBER OF FEMALE B6C3F1 MICE WITH ALVEOLAR/BRONCHIOLAR ADENOMA (2/50, 5/49, 10/50*) IS COMPLICATED BECAUSE OF A CONCOMITANT SENDAI VIRAL INFECTION (IN ALL GROUPS OF MICE).

[Bioassay Reports reviewed and evaluated at the 16 December meeting of the NTP Peer Review Panel. Available in about 12 weeks from the NTP Public Information Office, P.O. Box 12233, Research Triangle Park, NC 27709.]

PUBLISHED CARCINOGENESIS BIOASSAY REPORTS

Agaritine: Toth, B., Raha, C.R., Wallcave, L., and Nagel, D. Attempted Tumor Induction with Agaritine in Mice. Anticancer Research 1: 255-258 (1981). Agaritine, a constituent of the cultivated mushroom Agaricus bisporus, was administered at concentrations of 0 (100 male and 100 female), 0.0625 (50 male and 50 female), and 0.03125% (50 female) in drinking water for life to randomly bred Swiss mice. Under the conditions of this test, agaritine was reported not carcinogenic for Swiss mice of either sex. During the course of the experiment, however, a substantial number of animals exhibited convulsive seizures.

N-Nitrosodiethanolamine: Lijinsky, W., Reuber, M.D., and Manning, W.B. Potent Carcinogenicity of Nitrosodiethanolamine in Rats. Nature 288: 589-590 (11 December 1980). N-Nitrosodiethanolamine was made available in drinking water to groups of 10 male and 10 female F344 rats for about six months. The experiment was terminated at week 34. Dose levels equaled 0; 3,900; 7,800; 15,600; 31,250; and 62,500 ppm. All animals in the treated groups had hepatocellular carcinomas (the high dose was toxic, and these animals were not evaluated). None in the control group had these lesions.

January 1982

The Panel of Experts associated with the Technical Reports Review Subcommittee will continue to serve through fiscal year 1982. Five new members have been appointed to replace those members whose terms of service were completed. The new and continuing Panel members, and the Subcommittee members are:

Subcommittee Members

Dr. Margaret Hitchcock (Toxicology)
John B. Pierce Foundation Laboratory
New Haven, Connecticut

Dr. Alice S. Whittemore (Biostatistics)
Stanford University
Stanford, California

Dr. Curtis Harper (Pharmacology)
University of North Carolina
School of Medicine
Chapel Hill, North Carolina

Panel Members

Dr. Norman Breslow (Biostatistics)
University of Washington
Seattle, Washington

Dr. Bernard A. Schwetz (Toxicology)
Dow Chemical U.S.A.
Midland, Michigan

Dr. James Swenberg (Pathology)
Chemical Industry Institute
of Toxicology
Research Triangle Park,
North Carolina

Panel Members (Cont'd)

Dr. Robert M. Elashoff (Biostatistics)
Jonsson Comprehensive Cancer Center
Los Angeles, California

Dr. Joseph H. Highland (Chemistry)
Environmental Defense Fund
Washington, D.C.

Dr. Michael Holland (Pathology)
Oak Ridge National Laboratory
Oak Ridge, Tenessee

Dr. Frank Mirer (Toxicology)
United Auto Workers
Detroit, Michigan

Dr. Robert A. Scala (Toxicology)
Exxon Corporation
Linden, New Jersey

Dr. Stan D. Vesselinovitch (Pathology)
University of Chicago
Chicago, Illinois

Dr. Mary Vore (Pharmacology)
University of Kentucky
College of Medicine
Lexington, Kentucky

Seven recent NTP Technical Reports on the Carcinogenesis Bioassay of Caprolactam (TR 214); Cytembena (TR 207); Di(2-ethylhexyl)adipate (TR 212); FD&C Yellow No. 6 (TR 208); Locust Bean Gum (TR 221); 2,3,7,8-Tetrachlorodibenzo-p-dioxin (Dermal) (TR 201) and (Gavage) (TR 209) are available from the Public Information Office (TB), National Toxicology Program, Box 12233, Research Triangle Park, NC 27709. Requests must be accompanied by a mailing label.

PSORALENS -- Psoralen plus ultraviolet light (320-360 nm), referred to as PUVA therapy, is used as treatment for psoriasis. In the United States in 1978, an estimated 35,000 patients received such treatment in clinical studies under a FDA Investigational New Drug (IND) application. The FDA recommended that the NTP develop toxicology profiles on select psoralens because of their clinical use and because systemic animal toxicology studies have not been performed. The NTP is investigating the effects of psoralen compounds including the most widely used, 8-methoxypsoralen, with and without ultraviolet light. These studies include mutagenicity, pharmacokinetics and metabolism, skin enzyme levels, and long-term bioassays. As part of this program, the NTP will sponsor a conference "Toxicology of Psoralens" on March 1-3, 1982 at NIEHS, Research Triangle Park, NC. Further information about the psoralen project and conference can be obtained from Dr. June Dunnick, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709, (919-541-4811, FTS 629-4811).

CLEARINGHOUSE ON PHTHALATES -- A key recommendation made at the Conference on Phthalates held in Washington, D.C. in June 1981 was that the NTP should consider creating a clearinghouse of toxicological data on this class of compounds. NTP consulted with scientists from federal health regulatory and research agencies as well as with the Chemical Manufacturers Association, all of whom supported the clearinghouse and contributed to its development. The Environmental Protection Agency (EPA) is particularly committed to this project because of its involvement in the testing of alkyl phthalates under the Toxic Substances Control Act and together with the NTP sponsored the formation of the Clearinghouse. Persons or organizations planning, conducting, or having completed research on the toxicological effects of these compounds are requested to contact Ms. Joan Chase, NTP/EPA Clearinghouse on Phthalates, Room 3A-06, Landow Building, National Institutes of Health, Bethesda, MD 20205, 301-496-1152, FTS 8-496-1152.

NTP CONTRACT AWARDS, INTERAGENCY AGREEMENTS AND MASTER AGREEMENTS -- New NTP contracts and interagency agreements awarded through the fourth quarter of fiscal year 1981 are listed in Table 5. Fourteen contracts for toxicological and carcinogenicity studies of chemicals have been awarded to six laboratories under the Master Agreement (MA) mechanism (formerly Basic Ordering Agreement). Summaries of awards for the fourth quarter fiscal year 1981 are shown in Table 6.

NTP CHEMICAL REGISTRY HANDBOOK -- The recently printed first edition of the NTP Chemical Registry Handbook contains those chemicals scheduled for testing in the NTP Annual Plans, fiscal years 1979, 1980 and 1981, as well as those compounds for which literature summaries have been prepared. For each chemical the following data are entered: NTP number, CAS registry number, CAS Ninth Collective Index name, synonyms as listed in CHEMLINE, molecular formula, structural formula, references to Tables in the Annual Plans in which the chemical is listed, locators to NLM online data bases, and a notation that a literature summary has been prepared. The Handbook is available from the National Technical Information Service (NTIS) 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650). Orders must specify: NTP Chemical Registry Handbook and NTIS accession code number PB 82-142977.

BIOASSAY QUALITY ASSURANCE SEMINAR -- The NTP conducts toxicological and carcinogenesis bioassays of chemicals mainly through the use of extramural contracts. To insure the accuracy of the findings from these bioassays and to maintain high standards the NTP monitors the overall operation of the commercial laboratory by initiating annual program reviews, quarterly site visits, ad hoc visits by experts in various scientific disciplines, and periodic laboratory reports. All bioassay contracts require Good Laboratory Practices (GLP). This being a major objective, the NTP held their annual bioassay contractors retreat with Dr. J. Fielding Douglas, Chairperson, NIEHS, on September 28-30, 1981 in Allenberry, Pennsylvania. In attendance were project officers, discipline managers and principal investigators from the NTP and Tracor-Jitco (prime contractor) and principal investigators and quality assurance directors from contract laboratories.

The NTP/NCI Monitoring Guidelines for the Conduct of Carcinogen Bioassays, Technical Report No. 218, released June 1981, provides formal guidelines for monitoring the small rodent bioassays. Copies may be requested from the Public Information Office, National Toxicology Program, PO Box 12233, Research Triangle, NC 27709. Requests must be accompanied by a mailing label.

AVAILABILITY OF NTP/NCI TECHNICAL REPORTS -- An insert in this issue of the Bulletin contains a complete list of NTP/NCI Carcinogenesis Bioassay Technical Reports. Copies are available through the Public Information Office, at the above address. Priority for complete sets will be given to libraries. For individual requests, an address label for every five reports is necessary to expedite handling. Allow 6-8 weeks for shipping.

TABLE 5

NEW NTP CONTRACTS AND INTERAGENCY AGREEMENTS AWARDED THROUGH THE FOURTH QUARTER FY 1981

CONTRACTS

Mammalian Cell Transformation (seven contracts)

Dr. A. S. Tu
Arthur D. Little, Inc., Cambridge, MA
NO1-CP-1-5794; $848,254; 9/81-9/84

Dr. Robert Ting
Biotech Research Laboratories, Inc.
Rockville, MD
NO1-CP-1-5807; $386,247; 9/81-9/84

Dr. Judith Poiley
Litton Bionetics, Inc., Kensington, MD
NO1-CP-5797; $1,184,033; 9/81-9/84

Dr. Richard Kouri
Microbiological Associates, Bethesda, MD
NO1-CP-1-5758; $647,643; 9/81-9/84

Dr. Richard Kouri
Microbiological Associates, Bethesda, MD
NO1-CP-1-5795; $794,119; 9/81-9/84

Dr. Eugene Elmore
Northrop Services, Inc.
Research Triangle Park, NC
NO1-CP-1-5798; $761-663; 9/81-9/84

Dr. George Hatch
Northrop Services, Inc.
Research Triangle Park, NC
NO1-CP-1-5796; $719,247; 9/81-9/84

Development and Validation of a Multiple Endpoint Mutation System in Cultured Mammalian Cells (two contracts)

Dr. Grant Brewen
Allied Corporation, Morristown, NJ
NO1-CP-1-5764; $797,817; 9/81-9/85

Dr. Kenneth Loveday
Bioassay Systems Corp., Woburn, MA
NO1-CP-1-5809; $562,295; 9/81-9/85

Chromosome Damage Testing in Chinese Hamster Ovary Cells

Dr. P.S. Sabharwal
Environmental Health Research and Testing, Inc.
Lexington, KY
NO1-CP-1-5789; $216,756; 9/81-9/83

Sperm Morphology and Vaginal Cytology Evaluation

Dr. P.S. Sabharwal
Environmental Health Research and Testing, Inc.
Lexington, KY
NO1-ES-1-5011; $97,588; 9/81-3/83

Modification of the Salmonella Test for Chemicals That May be Metabolized to Mutagens under Reductive Conditions

Dr. Charles King
Michigan Cancer Center, Detroit, MI
NO1-CP-1-5762; $154,099; 9/81-9/83

Statistical Analysis of Bioassay Data

Dr. James Joiner
Program Resources Inc.
Research Triangle Park, NC
NO1-CP-1-5733; $933,715; 7/81-7/86

NTP Chemical Repository

Dr. Laurence Keith
Radian Corporation, Austin, TX
NO1-ES-1-5010; $2,786,992; 9/81-9/86

INTERAGENCY AGREEMENTS WITH THE DEPARTMENT OF ENERGY

Syrian Hamster Embryo Cell Transformation Validation

Dr. Elizer Huberman
Argonne National Laboratory, Argonne, IL
YO1-CP-1-0205; $954,417; 9/81-9/84

Spontaneous Chromosome Abberations and Sister Chromatid Exchanges in Human Lymphocytes (two agreements)

Dr. Michael Bender
Brookhaven National Laboratory, Upton, NY
YO1-CP-1-0204; $483-092; 9/81-9/84

Dr. Julian Preston
Oak Ridge National Laboratory, Oak Ridge, TN
YO1-CP-1-0203; $321,650; 9/81-9/84

Evaluation and Application of an In Vivo Mouse Assay for Chemically Induced Sister Chromatid Exchanges and Chromosome Abberations (two agreements)

Dr. Raymond Tice
Brookhaven National Laboratory, Upton, NY
YO1-CP-1-0207; $533,984; 9/81-9/84

Dr. Alfred McFee
Comparative Animal Research Laboratory, Oak Ridge, TN
YO1-CP-1-0206; $526,623; 9/81-9/84

NIOSH TECHNICAL REPORT: Teratologic Assessment of Butylene Oxide, Styrene Oxide and Methyl Bromide (No. 81-124, 76 pages, 1981). Groups of rats and rabbits were exposed by inhalation to each of these chemicals (butylene oxide - 250 and 1000 ppm; methyl bromide - 20 and 70 ppm; and styrene oxide - 100 and 300 ppm rats, 15 and 50 ppm rabbits) 7 hours per day through gestation day 19 (rats) or 24 (rabbits). Butylene oxide and methyl bromide caused little toxicity in rats; in rabbits, both concentrations of butylene oxide and the high dose of methyl bromide caused death. Neither induced marked embryotoxicity. Both styrene oxide doses to rats and to rabbits caused increased mortality; adverse toxic and developmental effects were observed. Availability: Publications Dissemination, NIOSH, Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, OH 45226.

TABLE 6

NEW TASK ORDERS AWARDED UNDER MASTER AGREEMENTS THROUGH FOURTH QUARTER FY 1981

TOXICOLOGICAL AND CARCINOGENICITY STUDIES IN LABORATORY ANIMALS

CONTRACTOR	CHEMICAL (CAS Registry Number) NTP Chemical Manager	STUDIES
BATTELLE COLUMBUS LABORATORIES COLUMBUS, OH		
Dr. A. Peters; NO1-CP-9-5653-03 $376,668; 9/81-9/82	o-Benzyl-p-Chlorophenol (120-32-1) Dr. L. Birnbaum	HUCC[1], Immunotoxicology, Neurotoxicology, Prophryins, Subchronic bioassay[2]
	Tricresyl Phosphate (1330-78-5) Dr. R. Irwin	Cholinesterase, Hematology, Neurotoxicology, Subchronic bioassay[2]
GULF SOUTH RESEARCH INSTITUTE BATON ROUGE, LA		
Mr. Ralph Wheeler; NO1-CP-0-5698-01 $72,920; 9/81-9/82	Manganese Sulfate (7785-87-7) Dr. D. Walters	Hematology, Manganese (liver), Subchronic bioassay[2]
Mr. Ralph Wheeler; NO1-CP-0-5698-02 $63,053; 9/81-9/82	Tetrahydrofuran (109-99-9) Dr. B. Gupta	Hematology, Subchronic bioassay[2]
HAZELTON LABORATORIES AMERICAN, INC. VIENNA, VA		
Dr. William Coate; NO1-CP-9-5655-02 $172,266; 9/81-9/82	Acetonitrile (75-05-8) Dr. J. McCoy	Hematology, Immunotoxicology, Radioimmunoassay, Urine cholinesterase, Subchronic bioassay[3]
Dr. Borge Ulland; NO1-CP-9-5655-03 $1,833,988; 9/81-9/85	C.I. Acid Red 114 (6459-94-5) C.I. Direct Blue 15 (2429-74-5) 3,3'-Dimethoxybenzidine (119-90-4) 3,3'-Dimethylbenzidine (119-93-7) Dr. J. Mennear	HUCC[1], Subchronic bioassay[2], Chronic bioassay (rat studies only)
Dr. Borge Ulland; NO1-CP-9-5665-01 $183,337; 9/81-9/82	1,2,3-Trichloropropane (96-18-4) Dr. J. Lamb	HUCC[1], Endocrinology, Sperm enumeration and morphology, Subchronic bioassay[3]
INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION MATTAWAN, MI		
Dr. Barrie Phillips; NO1-CP-0-5700-07 $68,645; 9/81-9/82	C.I. Direct Blue 218 (10401-50-0) Dr. J. Mennear	Hematology Clinical chemistries Subchronic bioassay[2]
Dr. Barrie Phillips; NO1-CP-0-5700-08 $115,425; 9/81-9/82	Propantheline Bromide (50-34-0) Dr. J. Dunnick	HUCC[1], Subchronic bioassay[3]
	Triamterene (396-01-0) Dr. C. Whitmire	HUCC[1], Subchronic bioassay[2]
LITTON BIONETICS, INC. KENSINGTON, MD		
Dr. Allan Manus; NO1-CP-9-5652-01 $392,967; 9/81-9/82	Methdilazine (1982-37-2) Dr. D. Goldman	Hematology Immunotoxicology Subchronic bioassay[3]
	Promethazine (60-87-7) Dr. M. Luster	HUCC[1] Immunotoxicology Subchronic bioassay[2]
RALTECH SCIENTIFIC SERVICES, INC. MADISON, WI		
Dr. G. Rao; NO1-CP-0-5696-01 $554,868; 9/81-9/82	Methylphenidate (113-45-1) Dr. W. Kluwe	Bone length and density Growth hormone Subchronic bioassay[3]
	Riddelliine (23246-96-0) Dr. D. Goldman	HUCC[1], Electron Microscopy, Pathology, Subchronic bioassay[6]
Dr. G. Rao; NO1-CP-0-5696-02 $145,984; 9/81-9/82	p-Nitroaniline (100-01-6) Dr. R. Chhabra	Bone marrow studies, Hematology, Subchronic Bioassay[3]
	o-Nitroanisole (91-23-6) Dr. R. Chhabra	Hematology, Urinalysis, Subchronic bioassay[2]

Species: Fisher 344 rats and B6C3F1 mice of both sexes
1 = hematology, urinalysis, clinical chemistries; 2 = acute; 14-day repeated dose, 90-day repeated dose;
3 = 14-day repeated dose, 90-day repeated dose; 4 = two-year (lifetime) bioassay; 5 = 120 day repeated dose with interim sacrifice
6 = 8 week repeat dose; 26 week repeated dose

NTP STAFF -- Ten scientists within the Toxicology Research and Testing Program, NIEHS/NTP, are now board certified diplomates of the American Board of Toxicology: Kamal Abdo, Gary Boorman, Rajendra Chhabra, June Dunnick, Joyce Goldstein, James Lamb, Robert Maronpot, Ernest McConnell, John Moore, and Ethard Van Stee.

Additions -- DR. LAWRENCE BOONE, Cellular and Genetic Toxicology Branch from the Biology Division, Oak Ridge National Laboratory -- DR. SANDRA BROWN, Program Operations Branch from the Bureau of Drugs, Food and Drug Administration -- DR. KENNETH CHU, Carcinogenesis and Toxicology Evaluation Branch from a one-year detail with the Health Standards Program, Occupational Safety and Health Administration -- DR. WILLIAM EASTIN, Carcinogenesis and Toxicology Evaluation Branch from the Fish and Wildlife Service, U.S. Department of the Interior -- DR. PATRICIA STRAAT, Program Operations Branch from the Division of Research Grants, National Institutes of Health -- DR. HANS WEBER, Guest Scientist, Carcinogenesis and Toxicology Evaluation Branch from the Institute of Technology, University of Zurich, Switzerland.

Transfers -- MR. THOMAS FISCHETTI and MS. SHARON LEENEY transferred to the Program Operations Branch, from the Technical Information Section.

Losses -- DR. LARRY LOMAX joined the faculty of the School of Veterinary Medicine, University of Georgia, Athens, GA -- DR. MARTIN PADARATHSINGH is now an Executive Secretary of the Pathology B Study Section, Division of Research Grants, National Institutes of Health --MR. DALTON TIDWELL joined Investment Management Services, Falls Church, VA.

[NTP Technical Bulletin Publication Schedule -- January, April, July, and October]

NTP Technical Bulletin
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